UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/270,437	03/16/99	CHEN	Y	LUD5538.1CIP

024972
FULBRIGHT & JAWORSKI, LLP
666 FIFTH AVE
NEW YORK NY 10103-3198

HM22/0605

EXAMINER	
CANELLA,K	
ART UNIT	PAPER NUMBER
1642	13

DATE MAILED: 06/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/270,437	Chen et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *53-109* is/are pending in the applica

4a) Of the above, claim(s) *74-79 and 85-107* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *53-73, 80-84, 108, and 109* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5, 6*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election with traverse of Group I, drawn to isolated nucleic acids, expression vectors, hosts, compositions and kits thereof. The traversal is on the grounds that the restriction is defective as the claims of Group V, drawn to methods for detecting and monitoring pathological conditions including cancer, should be included as these claims are a method of use of the nucleic acids of Group I. Further, applicant argues that the use of nucleic acids in an in vitro mutagenesis assay is unknown in the art. This has been considered but not found persuasive. Firstly, in vitro mutagenesis assays are well known in the art as exemplified in part by the papers of Seo et al (Mutation Research, 2000, Vol. 463, pp. 215-246) and Hruszkewycz et al (Carcinogenesis, 1991, Vol. 12, pp. 2185-2187). Secondly, the inventions of Group I and V can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product of Group I can also be used to make the product of Group II. As to the question of burden of search, the claims of Groups I and V are classified differently, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group.

However, the policies set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86 will be followed. Method claims limited to the scope of the allowable product claims will be rejoined and examined at the time the product claims are indicated as being allowable.

For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

2. Claims 1-52 are canceled. Claims 53-109 are pending. Claims 74-79, and 85-107, drawn to non-elected inventions, are withdrawn from consideration. Claims 53-73, 80-84, 108 and 109 are examined on the merits.

Claim Objections

3. Claim 80 is objected to because of the following informalities: the claim is dependent upon a non-elected claim. Appropriate correction is required.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 53-73, 80-84, 108 and 109 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific substantial asserted utility or a well-established utility. The instant claims are drawn to the polynucleotide sequences of SEQ ID NO:5-8 which encode a protein. The specification teaches that the polynucleotide of SEQ ID NO:1 (expressed from the CTL7 gene) was found in normal testis, and the cancerous tissues enumerated in Table 3. The specification teaches that KOC-2 and KOC-3 genes were identified from the melanoma cell line SK-MEL-37 by screening a recombinant expression library obtained from this cell line with allogenic patient serum. When the patterns of expression of KOC-2 (SEQ ID NO:5 and SEQ ID NO:7) and KOC-3 (SEQ ID NO:6 and SEQ ID NO:8) was determined, it was found that KOC-2 was detected in the normal testis (pg. 14, lines 3-4) and KOC-3 was universally expressed in normal tissues with the testis having the highest level of expression. KOC-3 was also found to be overexpressed in several melanoma cell lines (pg. 14, lines 9-11). However, the specification fails to demonstrate a utility for the nucleic acids of SEQ ID NO:5-8, as the specification fails to correlate the presence of the protein encoded by SEQ ID NO:5-8 in clinical samples. The use of the SEREX system to identify antigenic proteins is not a guarantee that the protein is actually expressed as an antigen in a patient as part of a disease process, as it is known in the art that

antibodies bind to epitopes on proteins and antibodies can cross react with different proteins containing the same or similar epitopes. For instance, the KOC-3 polynucleotide may not normally be translated into a KOC-3 polypeptide as it is known in the art that expression of mRNA does not dictate the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not necessarily contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Therefore, one of skill in the art would not rely on the expression of the polynucleotides of SEQ ID NO:5-8 as evidence of the expression of the corresponding encoded proteins. Furthermore, under conditions of recombinant expression, epitopes of KOC-2 and 3 which are not normally expressed in a patient within the context of MHC could be expressed by E. Coli. If one of these epitopes cross-reacts with allogenic patient serum, it cannot be concluded with certainty that the protein is expressed in said patient. Further, even if the KOC-2 or 3 polypeptides are expressed in a human patient at levels commensurate with the abundance of the KOC-2 or 3 polynucleotides, the data indicating that the KOC-2 polynucleotide was restricted to the normal testis and that the KOC-3 polynucleotide was

universal in normal tissues implies that a patient would not have a specific antibody toward the KOC-2 or 3 polypeptides due to immunogenic tolerance toward the peptides (Abbbas, et al, Cellular and Molecular Immunlogy (textbook), 1991, pp. 207-208).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 53-73, 80-84, 108 and 109 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial credible asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

8. In the event that Applicants might be able to overcome the 35 USC 101 rejection above, the specification would still be enabling only for claims limited to polynucleotides comprising SEQ ID NO:5-8, the complete complement of said polynucleotides, vectors and host cells thereof, and a method of producing polypeptides encoded by SEQ ID NO:5-8 because the specification does not reasonably provide enablement for polynucleotides encoding proteins that hybridize to SEQ ID NO:5-8 or to compositions comprising expression vectors encoding an 8 to 25 amino acid sequence. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

(A)As drawn to polynucleotides which hybridize to SEQ ID NO:5-8.

Claims 53, 71, 72, 73 encompasses polynucleotides encoding proteins, said polynucleotides comprising non-disclosed nucleic acid sequences that hybridize to SEQ ID NO:5-8 under non-disclosed stringent conditions. Clearly, since the specification has not taught how to use said polynucleotides for the reasons given in paragraphs 4 and 6 supra, the specification has

not enabled the scope of claims 53 and 71-73 which are drawn to polynucleotides encoding proteins that hybridize to SEQ ID NO:5-8 under stringent conditions. The specification teaches stringent conditions for Southern blotting experiments (pg. 11). However, the description of the hybridization conditions is not limiting as polynucleotides encoding proteins can comprise small oligomers which can hybridize to the disclosed SEQ ID NO:5-8. When given the broadest reasonable interpretation, the claims are clearly intended to encompass a variety of species including full-length cDNAs, genes and protein coding regions and it would be expected that a substantial number of the hybridizing or complementary polynucleotides encompassed by the claims would not encode polypeptides having structural or functional similarities with the putative polypeptides encoded by SEQ ID NO:5-8. For example, Accession Number C03267, representing Human Secreted Protein 5' EST, could hybridize under stringent conditions to SEQ ID NO:6 and Accession Number AF117106, representing the polynucleotide encoding IGF-II mRNA binding protein 1, could hybridize to SEQ ID NO:5, but the specification fails to provide an enabling disclosure for how one would use such polynucleotides. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art on how to use the broadly claimed species. For the above reasons, undue experimentation would be required to practice the claimed invention.

(B)As drawn to expression vectors encoding 8-25 amino acids

Claims 80-84 are drawn to compositions comprising expression vectors encoding at least one peptide consisting of an amino acid sequence from 8 to 25 amino acids derived from polypeptides encoded by the polynucleotides of SEQ IDNO:5-8. However, the specification make no mention of particular regions of the proteins encoded by SEQ ID NO:5-8 which would have a particular function, for instance as an epitope. Furthermore, the specification does not teach polynucleotides encoding B-cell epitopes vs polynucleotides encoding T-cell epitopes. Given the hypothetical protein sequences encoded by the polypeptides of SEQ ID NO:5-8, one of skill in the art would not be able to anticipate "epitopes" without undue experimentation. For instance, Paul (Fundamental Immunology (text) pg. 249-251) teaches that for the determination of immunogenicity of certain regions of a protein, knowledge of the three dimensional structure of

the protein is required to ascertain which polypeptides in a given protein would be accessible on the surface of the protein in order for the putative antigenic determinant to be bound by the antibody. In addition, Paul states that mobility of the putative antigenic determinant within the native protein structure is also a determining factor for the binding of the antigenic determinant to an antibody. Paul points out (pg. 250, lines 4-8) that "Measurement of the mobility in the native protein is largely dependent on the availability of a high resolution crystal structure, so its applicability is limited to only a small subset of proteins." Thus, the determination of an "epitope" is clearly a non-trivial enterprise, and without further guidance from the specification on known sequences of the BS265 peptide which have been determined to be epitopes in a specific organism, it would require undue experimentation for one of skill in the art to make and use the invention as claimed.

Claims 108 and 109 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This application contains sequence disclosures in the specification and in the claims, that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 since neither the paper copy of the Sequence Listing not the CRF includes SEQ ID NO:9-14.

Applicant is given the response period of this office action within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Applicant is requested to return a copy of the attached Notice to Comply with the reply.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 80-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 80 is vague and indefinite in the recitation of "an amino acid sequence of from 8 to 25 amino acids concatenated to each other in the isolated cancer associated antigen of claim 74". How this concatenation of undefined amino acids is supposed to occur within the context of the polypeptide encoded by SEQ ID NO:5-8 is unclear. For purpose of examination the claim will be read as --expression vector comprising a polynucleotide encoding 8 to 25 amino acids of the protein encoded by SEQ ID NO:5-8--.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
May 18, 2001

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600